



A Non smoker presenting as small cell carcinoma: A Rare case report

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Abstract

Once regarded as a smoker's disease, small-cell lung cancer (SCLC) has been occasionally detected in non-smokers as smoking rates decrease worldwide. We investigated the clinical and genetic characteristics of SCLC in non-smokers. Non-smokers with SCLC are increasingly prevalent and have a better prognosis than smokers with SCLC. We intend to publish this case due to rarity of the case presentation High index of suspicion should be kept for the possibility of diagnosing SCLC in non smokers so that these cases might not be misdiagnosed .

Keywords: Small-cell lung cancer, never-smoker, survival, next-generation sequencing, epidermal growth factor receptor mutation

Introduction

There are two broad categories of lung cancer: small cell lung cancer (SCLC) and non small cell lung cancer (NSCLC). SCLC, which is a highly malignant tumor derived from cells exhibiting neuroendocrine characteristics, accounts for 15% of lung cancer cases. NSCLC, which accounts for the remaining 85% of cases, is further divided into three major pathologic subtypes: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Adenocarcinoma by itself accounts for 38.5% of all lung cancer cases, with squamous cell carcinoma accounting for 20%, and large cell carcinoma accounting for 2.9%.^{1,2}In the past several decades, the incidence of adenocarcinoma has increased greatly, and it has replaced squamous cell carcinoma as the most

prevalent type of NSCLC. Small-cell lung cancer (SCLC) is known to be clinically different from non-small-cell lung cancer (NSCLC) in its high response rate to first-line chemotherapy, early progression, and overall poor prognosis. In addition, smoking is universally understood to cause SCLC, and no targetable oncogene has been found in SCLC. Although lung cancer is commonly viewed as a smoker's disease, ~15%–20% of all lung cancer cases worldwide develop in non-smokers³. The prevalence is also different histologically and geographically. The proportion of non-smokers is higher among Asian patients with NSCLC than in non-Asian patients. In addition, never-smokers are more often diagnosed with adenocarcinoma than smokers [5]. While the

proportion of non-smokers in lung cancer varies geographically, it seems to be gradually increasing worldwide.

Although the reason for the increase remains unknown, the research into lung cancer in never-smokers has become increasingly important as the smoking rates decrease worldwide.

Unlike NSCLC, studies on the genetic characteristics of SCLC are rare, and no targetable oncogene has been reported. In an era when many target agents are waiting to be used in clinical trials and the methods to find the potentially target gene are available, comprehensive genetic analysis in the appropriate population is urgently needed. It has been reported that a few never-smokers have SCLC harboring epidermal growth factor receptor (EGFR) mutations, and some responded to EGFR tyrosine kinase inhibitors (TKIs)^{6,7} However, there are insufficient data regarding how many de novo SCLC cases in never-smokers involve an EGFR mutation and whether these mutations can be targeted in the treatment of SCLC. In addition, there are only two studies evaluating the prognostic relevance of smoking status in SCLC, which were carried out in a primarily non-Asian population. The evaluation of genetic and clinical characteristics of SCLC in never-smokers likely will be more effective and relevant when carried out in a region of endemic nonsmoking-related lung cancer cases such as Korea or other Asian countries versus those studies carried out in other geographic areas.

Case History

A 60 year old male came to outpatient department of Chest and TB hospital, Amritsar with complaints of right sided chest pain, dry cough, breathlessness for the last 2 months. Patient also

gave history of noticing swelling right supraclavicular region and loss of appetite, generalized tiredness for past 1 month. Breathlessness was gradually progressive & now he was dyspneic on exertion. He had no history of orthopnea or paroxysmal nocturnal dyspnea. He had history of right sided chest pain for 15 days aggravated on cough and radiated to back.

No history of sweating, palpitation, smoking or exposure to known carcinogens. There was no family history of malignancy. He took 9 months treatment for pulmonary tuberculosis under RNTCP in the past.

On physical examination patient was having pallor & clubbing (grade 2). BP-140/90 mm Hg, Pulse rate – 88/min, Respiratory rate – 18/min.

On Respiratory system examination, shape of the chest was symmetrical on both sides. Movements of chest decreased on the right side of the chest, trachea central in position. On Palpation- Patient was febrile with tenderness over right side chest, Chest movement & expansion decreased right side of chest, Vocal fremitus – decreased on right side of chest mammary area. Percussion note was dull note on right side of chest mammary area. On auscultation, breath sounds decreased on right side of chest mammary area with no added sounds. Breathing on the left side was vesicular without any accompaniments.

Hematology and blood chemistry were within normal limits. HIV was non reactive. Ultrasound abdomen revealed no abnormality. He was started on empirical antibiotics, bronchodilators and analgesics.

Chest x ray shows mediastinal widening along with hilar lymphadenopathy (Fig 1)

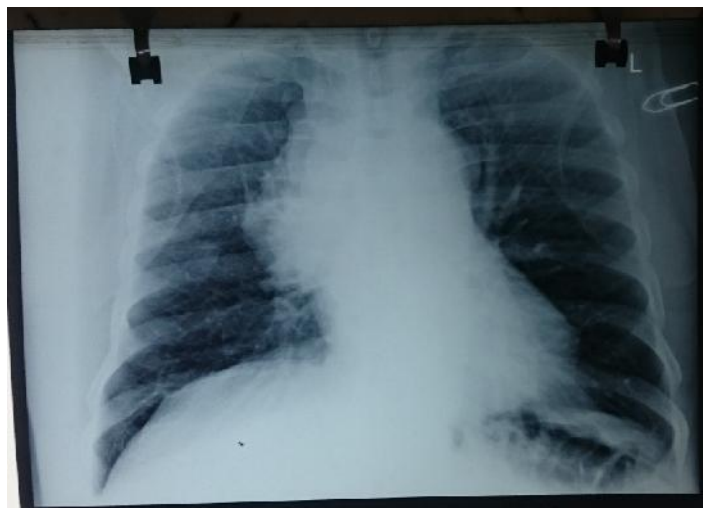


Fig 1: Chest xray

CECT chest revealed central mass at level of right main bronchus in close proximity to the

carina and there was mediastinal and hilar lymphadenopathy. (Fig 2)

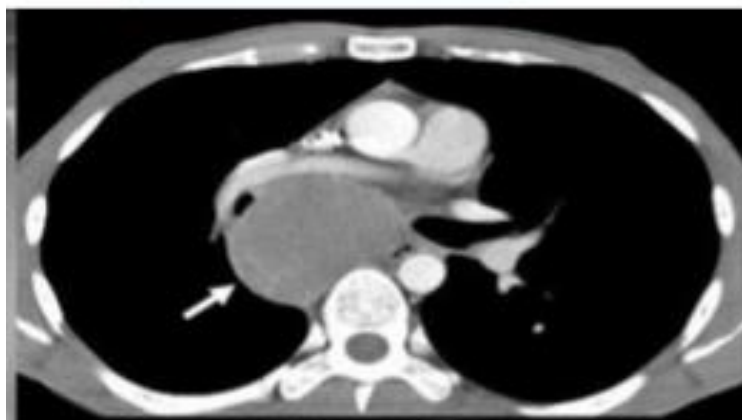


Fig 2 : CECT Chest

Discussion

Lung cancer remains the leading cause of cancer mortality, accounting for more deaths than breast, colon, and prostate cancer combined. The primary etiologic agent responsible for SCLC is tobacco smoke. Moreover, smoking is associated with both lung cancer carcinogenesis and the prognosis of lung cancer patients. Due to the overwhelming etiological role of tobacco smoking, lung cancer is mainly considered a smoking-related disease; consequently, the never-smoker population is usually under-represented in lung cancer studies. Only recently has attention turned toward the small number of never-smokers with this disease. Smoking status is important in comprehensive treatment of lung cancer, including anti smoking

education. Tobacco smoking is the most important modifiable risk factor for lung cancer. It has been estimated that up to 20% of all cancer deaths worldwide could be prevented by the elimination of tobacco smoking⁸.

Never smokers are defined as persons who have smoked fewer than 100 cigarettes in their life time, including life time nonsmokers. An estimated 15 % of lung cancers in men and upto 53 % in women worldwide occur in never smokers, accounting for 25 % of all lung cancer cases⁹. Lung cancer in never smokers considered as a distinct group would rank as the seventh most common cause of cancer death worldwide, ahead of cervical, pancreatic, and prostate cancer.¹⁰

In the present case the patient had no history of smoking, however we could not rule out the possibility of second-hand smoking effects, as this could be an important factor in SCLC. The right supraclavicular lymphadenopathy (Stage N3) and chest xray findings of mediastinal widening along with lymphadenopathy prompted us to do CECT chest.

CECT chest showed central mass at level of right main bronchus in close proximity to the carina and there was mediastinal and hilar lymphadenopathy.

CT guided FNAC was done and light microscopy revealed homogenous cell population with salt and pepper chromatin and moderately prominent nucleoli and a diagnosis of small cell lung carcinoma was made. SCLC is a malignancy that is sensitive to radiation and our patient was started on thoracic radiation therapy and chemotherapy.

Chemotherapy was initiated with cisplatin and etoposide and the patient is currently under our follow up.

Conclusion

Never-smokers with SCLC are increasingly prevalent and have a better prognosis than smokers with SCLC in our study group. High index suspicion should also be kept for the possibility of diagnosing SCLC in non smokers so that these cases might not be misdiagnosed.

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